ORIGINAL ARTICLE

Comparison of cerebral blood flow pattern by transcranial Doppler in patients with diffuse and focal causes of brain death

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Background: This study aims to assess the cerebral vessels flow in brain death patients with different causes, including focal and diffuse lesions and comparison of flows according to the underlying causes. **Materials and Methods:** Two groups of 15 brain-dead patients one with focal and the other with diffuse brain lesions were compared according to their cerebral blood flow pattern 48 h passed brain death certification. **Results:** Bilateral absence of flow in middle cerebral artery (MCA) was found in 54.5% of brain-dead patients with diffuse lesion and 50.33% of those with focal lesions. Systolic spike pattern in MCA flow was found in 46.2% of patients with focal lesion and 16.65% of patients with diffuse lesion. Diastole–systole separation pattern in MCA was seen in 16.65% of patients with the diffuse lesions. This pattern in MCA was not seen in patients with the focal lesion group. In carotid arteries, we did not find the absence of flow in any cases. Thirty percent of all patients in both groups had a normal flow pattern (36.6% of patients with focal lesions and 23.3% of patients with diffuse lesion). Patients with focal lesion had 33.3% systolic spike pattern flow and had 23.35% diastole–systole separation flow pattern. In intra-cranial vessels, systolic spike pattern was more common among patients with focal lesions than patients with diffuse lesion, however, this difference was not statistically significant (46.2% of patients with focal lesion and 16.65% of patients with diffuse lesion) (*P* value = 0.244-0.09). Diastole–systole separation flow was more common in patients with diffuse lesions than those with the focal lesions although this could not reach the significant level as the previous pattern (20% of patients with diffuse lesion versus no case in patients with focal lesion) (*P* value = 0.181). **Conclusion:** Absence of flow was the most common brain flow pattern in the focal and diffuse group lesions. There was no difference in flow pattern between the focal and diffuse brain lesions groups in brain-dead patients.

Key words: Blood flow pattern, brain death, diffuse brain lesion, focal brain lesion

INTRODUCTION

In our world, brain death (BD) is accepted as an indicator of the end of life in its physical form. BD is defined as irreversible cessation of all brain functions.[1] According to the concept of BD, diagnosis of BD demands certification of cessation of cerebral blood flow associated with the absence of brain and brainstem activity verified by clinical examination.[2] The essential feature of flow abnormality is brain tamponade, which is the arrest of blood circulation in brain caused by intra-cranial hypertension.[3]

According to Shiogai and Takeuchi[4] study there is an interval of 24 h or less since the arrest of brain blood circulation and BD certification. Transcranial Doppler (TCD) is one of the most appreciated methods for determining absence or flow abnormality.[5,6] This method is superior to electroencephalogram (EEG) or clinical exam concerning BD certification in barbiturate therapy or hypothermia, which preclude proper diagnosis by those two methods.[7]

According to a research done by neurosonology group of the world federation of neurology, the absence of signal leads to a limitation the method, especially in old women in whom the poor temporal window is found, so criteria of systolic spike or oscillating flow in internal carotid arteries (ICA) and common carotid artery (CoCA) or posterior cerebral arteries (typical extra-cranial signals) can be justified as a proof for BD certification in difficult cases.[8] Lampl *et al*.[9] studied transorbital approach as a diagnostic approach for BD verification.

Dominguez-Roldan *et al*.[10] used carotid siphon via the transorbital window for difficult cases with poor temporal window. Poularas *et al*.[3] compared TCD with contrast angiography in BD patients study, and their results were same in both methods. In that study, TCD

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was approved as a sensitive indicator of BD and an alternative for standard angiography. In Dominguez-Roldan *et al*.[2] studies there was a comparison between supratentorial and infratentorial lesions flow pattern in brain-dead patients. In patients with supratentorial lesions, the predominant pattern was reverberating flow, while in patients with infratentorial lesions, systolic spike pattern was the most frequent. The addition of insonation of cervical ICA and of the siphon increased sensitivity of TCD.

Nevertheless, a cerebral circulation arrest (CCA) flow pattern may appear later on these segments.[11] In case of CCA confirmation, the Doppler waveform has to be considered rather than mean flow velocity.[12] In a recent study, TCD was used as a first line ancillary test to confirm BD when clinical examination was not conclusive. The kind of management and evaluation would change according to detection of CCA in any major vessels.[13] In another study, its found that early use of TCD allows to stop all critical care, avoiding prolonged artificial life support and to speed up the organ donation procedure.[14] TCD was used in this study as a confirmatory test for BD after clinical examination points to this event. This test has unique advantage of being non-invasive, non-radioactive and relatively non-expensive bedside technique and one that can be repeated readily, but in our idea it cannot be useful when the clinical exam finds some brain or brainstem function or reflexes.

Dominguez *et al*. studied about Doppler waveforms in supratentorial and infratentorial causes of BD. We decided to compare Doppler waveform in the focal and diffuse causes of BD patients for earlier diagnosis of BD and facilitation of the diagnostic process of BD, which is the prerequisite of organ donation.

We decided to compare the flow pattern between diffuse and focal causes of the supratentorial lesions in brain dead patients.

MATERIALS AND METHODS

Thirty patients admitted in intensive care unit with clinical and paraclinical criteria of BD as mentioned by American Academy of Neurology,[15] underwent cerebral flow assessment. All cases were examined by neurologists twice a day and paraclinical tests such as brain computed tomography (CT) scan or magnetic resonance imaging (MRI), and EEG were used commensurately before BD certification. Patients with any focal lesions in brain CT or MRI would be placed in the "focal group" and otherwise in the "diffuse group" (such as hypoxia, diffuse axonal lesion, and poisoning). The diagnosis of BD was performed according to the definition of BD; absence of neurological function in brain stem and hemispheres that was associated with the absence of bioelectrical activity and cessation of cerebral blood flow.[2] The study was performed by TCD for all patients with certified clinical BD and below 3 μV amplitude EEG.

Mean flow velocity, peak systolic velocity, end diastolic velocity, and pulsatility index of all extra- and intra-cranial vessels were checked by means of TC-22 legend TCD manufactured by Nicolet vascular system (Viasys Healthcare, Inc.). For flow detection, 4 MHz transducer was used for extra-cranial vessels, and 2 MHz transducer was used for intra-cranial vessels. The depth of the measurement was matched with the highest signal in each intra-cranial artery. All these velocities were measured by centimeters per second. Our aim of the study was considering flow-pattern and not velocities and indices.

Following sonographic patterns constitute cerebral circulatory arrest: (1) systolic spike pattern (without diastolic flow), (2) reverberating flow pattern (brief systolic forward flow and diastolic reverse flow), (3) diastole–systole separation pattern (systolic forward spike flow and diastolic flow with separation), and (4) no flow pattern.[2]

All types of flow patterns found in vessels were carefully studied and recorded in tables. We left 48 h window between clinical certification of BD and TCD for more accuracy of study. As some researches found, early false-positive TCD findings could be seen shortly after cardiac arrest and in acutely raised intra-cranial pressure due to bleeding from an aneurysm with the flow arrest patterns similar to those seen in CCA.[16,17] On the other hand, we did not decide to confirm efficacy of TCD for early diagnosis in this study but rather to compare the flow patterns in two groups of BD patients. Otherwise false negative TCD in early phase of BD could also alter our results.

We analyzed the result of each artery study according to the cause of BD in that case (focal or diffuse). Afterwards, all the results were compared with each other. The data were analyzed by means of SPSS version 16. Fisher-exact test was used to compare flow patterns between two groups. We chose the P value of 0.05 as a statistically significant cut of point.

RESULTS

The mean and standard deviation (SD) of age among patients were 40.46 ± 20.66. The main cause of brain damage was head trauma (contusion and diffuse axonal injury, hematoma) in nine patients, six patients had intra-cerebral hemorrhage, five patients had brain tumor or metastasis, three patients had major ischemic stroke, two patients were diagnosed with hypoxia, two patients

were diagnosed with poisoning, two patients were diagnosed with hypoxia after cardiac arrest, one patient had amniotic fluid emboli [Table 1]. Six patients were female (20%), mean and SD of age was 61.33 ± 20.16 and 24 patients were male (80%), their mean and SD of age were 35.25 ± 17.54. After analyzing axial computerized scan 15 patients (50%) had focal lesion, with mean and SD age of 34.00 ± 17.63 and 15 had diffuse lesions with mean and SD age of 46.93 ± 21.99.

Absence of flow was the most common flow pattern found in intra-cerebral arteries by TCD. The second common flow pattern was systolic spike flow. Diastole–systole separation pattern was the third common flow. The least frequent flow was reverberating flow pattern. The most common cause of admission was head trauma in our patients.

In CoCA, absence of flow was not seen in any cases. Thirty percent of common carotid flow patterns in our patients were normal.

The second common flow pattern was the systolic spike pattern. Diastole–systole separation pattern was the third common flow pattern. Reverberating flow pattern was the least common type found. The time of cardiac arrest was less than 14 days after BD certification but most of them died within the first week. It means that survival period of BD patients was shorter when extra-cranial vessels showed abnormalities of intra-cranial vessels.

Table 1: Causes of brain death in our patients

Focal brain lesion	Number	Diffuse brain lesion	Number
Hematoma, contusion	1	Hypoxia	4
Intracerebral hemorrhage	6	Diffuse axonal injury	8
Ischemic stroke	3	Poisoning	2
Brain tumor or metastases	5	Amniotic fluid embolism	1

We could not find significant results in-favor of any relationship between cerebral flow pattern and focal or diffuse cause of BD. The frequency of reverberating flow pattern in all cerebral vessels of our cases (both groups) was 6.6-6.7%. In our study the frequency of systolic spike flow pattern was 13.3-46.2%. Diastole–systole separation pattern frequency was up to 20% in diffuse lesions. Absence of flow was seen in 46.2-73.3% of our cases according to various vessels that have been studied. The comparison of flow patterns between two groups of patients is shown in Tables 2 and 3 with details.

Normal flow was seen only in CoCAs. Absence of flow was not seen in CoCAs. The results of both CoCAs measurements in all patients are shown in this part [Table 2]. About 70% of patients had abnormal CoCA flow. All of them had a shorter survival period than other patients with normal cervical blood flow.

Systolic spike flow was seen in intra-cranial vessels more in patients with focal lesions than patients with diffuse lesions, although significant results were not achieved. Diastole–systole separation pattern in intra-cranial vessels was more common in patients with diffuse lesions than patients with focal lesions, although significant results were not found. The results in right and left MCA of all cases are shown in Table 3 for concision.

DISCUSSION

Finding clues concerning with BD verification is one of the most important aims of medical personals in all units with admission of comatose patients. Before complete arrest of cerebral vessels flow there are some changes in flow pattern that help us for sooner detection of BD occurrence.

In this study, we decided to follow flow pattern changes in BD patients with different pathogenesis especially those

Table 2: Types of flow patterns in right and left common carotid arteries of brain dead patients

Brain lesion	DSSP		Normal		RFP		SSP		Total	
	R	L	R	L	R	L	R	L	R	L
Diffuse (%)	4 (26.7)	3 (20)	3 (20)	4 (26.6)	1 (6.7)	1 (6.7)	7 (46.6)	7 (46.6)	15 (100)	15 (100)
Focal (%)	4 (26.7)	3 (20)	5 (33.3)	6 (40)	1 (6.7)	1 (6.7)	5 (33.3)	5 (33.3)	15 (100)	15 (100)
Total (%)	8 (26.6)	6 (20)	8 (26.6)	10 (33.3)	1 (3.3)	2 (6)	12 (40)	12 (40)	30 (100)	30 (100)
P value	(1.0)	(1.0)	(0.6)	(0.69)	(1.0)	(1.0)	(0.7)	(0.7)		

DSSP= Diastole–systole separation pattern; RFP= Reverberating flow pattern; SSP= Systolic spike pattern; R= Right; L= Left

Table 3: Types of flow patterns in right and left middle cerebral arteries of brain dead patients

Brain lesion	No flow		DSSP		RFP		SSP		Total	
	R	L	R	L	R	L	R	L	R	L
Diffuse (%)	8 (53.3)	10 (55.7)	3 (20.0)	2 (13.3)	1 (6.7)	1 (6.7)	3 (20.0)	2 (13.3)	15 (100)	15 (100)
Focal (%)	6 (46.6)	6 (46.2)	0 (0)	0 (0)	1 (7.7)	1 (7.7)	6 (46.2)	6 (46.2)	13 (100)	13 (100)
Total (%)	14 (50.0)	16 (57.1)	3 (10.7)	2 (7.1)	2 (7.1)	2 (7.1)	9 (32.1)	8 (28.6)	28 (100)	28 (100)
P value	(1.0)	(0.44)	(0.18)	(0.48)	(1.0)	(1.0)	(0.24)	(0.09)		

DSSP= Diastole–systole separation pattern; RFP= Reverberating flow pattern; SSP= Systolic spike pattern; R= Right; L= Left

with diffuse lesions and others with focal underlying causes in order to find significant differences in their flow pattern as Dominguez did in comparison of supratentorial with infratentorial causes of BD only in one artery.[2] We studied most of the cerebral arteries in our patients and compared their flow pattern in both groups. Most of our patients were young, so we had fewer problems about old patients with a poor temporal window. We had ten patients above 55 years old of which 50% of them had detectable flow through the temporal window. Only five patients had no flow in their temporal window, four of whom were men between 56 and 61 years old. In male patients poor temporal window is less than women, and it could be found in a higher age than women. Only in a 79-year-old female the exact differentiation between absence of flow and poor temporal window was not possible.

In our study, systolic spike flow was seen more frequently inpatients with focal lesions.

In Dominguez study this flow pattern was also seen in both forms of focal lesions.

Our study showed that these four types of flow pattern could be found in all causes of BD. Diagnosis was based on finding one of these patterns rather than specific types of these abnormalities in each form of causes. Therefore, each one of these flow patterns could be a sign of BD.

In Carber study, TCD of middle, anterior and posterior cerebral arteries were considered as intra-cranial vessels study not intra-cerebral vessels, but all part of these vessels cannot be considered as extra-cerebral vessels.[18] In our study abnormality of flow pattern was found in all vessels.

Carber's idea about BD diagnosis to the effect that there always is an absence of flow pattern as seen in angiography, will not be generally valid due to some of BD patients having abnormal flow patterns instead of circulation absence.

In cases with the normal flow patterns, we must be suspicious about BD confirmation. As far as the normal flow pattern is found in cerebral vessels, it should be interpreted against BD verification. In other studies the patient with a persistent flow was considered as BD, there is a pre-phase of BD not an established phase of BD as mentioned later.

According to Dosemeci *et al*., if TCD is used after certification of BD, mostly no false-positive result could be found as in our study, but if it was used before clinical establishment in first 24 h of BD incidence, it may show normal flow, therefore those reports of persistent flow could be referred to this period.[19]

Unlike Dosemeci *et al*. we did not consider the absence of flow in first trial as the poor window in our young patients, because the poor window is seen in old patients usually ≥ 50 year old, and also more in women than men. Therefore, we considered absence flow in our findings as significant results when it was bilateral or persisted in three arteries more than 3 min.

In that study, the sensitivity of test was 98% on the 2nd day and reached 100% by the 4th day. We studied our patients after 48 h of BD signs occurrence for more sensitivity.

In windows other than temporal window, the absence of flow was considered as no flow in them. We did not seek the approval of TCD for BD certification.

In cervical region, ICA is also studied in our study as CoCA. One may prefer to evaluate the change of ICAs flow instead of CoCAs flow in cervical part, but in this part, as you know, the ICA has intra-cranial portion, so it cannot be thoroughly considered as a cervical vessel totally. Our finding about persistence of flow in cervical part is more related to CoCA than ICA as a part of it is in intra-cranial space and have no flow in different parts of it in some of our cases.

Therefore, abnormality in extra-cranial arteries can demonstrate more severity of the condition in our patients as mentioned later.

Another finding in this study that has not been reported yet, was shorter time of cardiac function in those patients who had an abnormality of CoCA flow in comparison to cases who have normal CoCA flow.

According to these findings, we offer further study including more cases considering CoCA flow pattern and maintenance of cardiac patients in BD patients after BD certification.

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